

REMARKS/ARGUMENTS

Specification

A paragraph has been added following paragraph [0010]. No New Matter has been added by this amendment. The paragraph summarizes information that is commonly known to people working in Chemistry, Biochemistry, and Nutrition.. Additionally, the paragraph is material contained in the following research papers that were incorporated by reference in the original Specification.

The molecular weights of the tocotrienol isomers can be calculated from the chemical structures of the molecules in “Pearce, B. C., R. A. Parker, M. E. Deason, A. A. Qureshi, and J. J. Wright, 1992, Hypocholesterolemic activity of synthetic and natural tocotrienols. J Med Chem 35:3595-3606” (Exhibit 1).

Page 3596, left column, chart I (top figure) shows the structure of tocotrienol with a table of possible methylation for the different isomers. This figure allows the calculation of the molecular weights for tocotrienol.

Page 3602, right column, paragraph 4, lines 1 and 5 shows a molecular weight of 424 Daltons for alpha-tocotrienol.

Page 3602, right column, paragraph 5, lines 1 and 5 shows a molecular weight of 410 Daltons for gamma-tocotrienol.

Page 3602, right column, paragraph 6, lines 1 and 5 shows a molecular weight of 396 Daltons for delta-tocotrienol.

The molecular weights of the tocotrienol and tocopherol isomers can be calculated from the chemical structures of the molecules in “Yu, C. C., M. Simmons-Menchaca, A. Gapor, B. G. Sanders, and K. Kline, 1999, Induction of apoptosis in human breast cancer cells by tocopherols and tocotrienols. Nutr Cancer 33:26-32” (Exhibit 1).

Page 27, Figure 1A, top structure is tocopherol and structure below is tocotrienol. The table below the structures explains the possible methyl substitutions for all of the isomers of tocopherol and tocotrienol.

The molecular weight of geranyl geraniol can be calculated from the chemical structure of the molecule in "Craveiro, A. A., et al., 1989, The Presence of Geranylgeraniol in *Bixa Orelana Linn.*," Quimica Nova, 12(3):297-298" (Exhibit 1).

Page 297, Bottom of left column shows the structures of Bixins. This figure allows the calculation of the molecular weights for Bixin, Isobixin, and Nor-Bixin. Bixin has a molecular weight of 394 Daltons.

Page 298, Top of left column shows the structure of geranyl geraniol. This figure allows the calculation of the molecular weight for geranyl geraniol. Geranylgeraniol has a molecular weight of 394 Daltons.

Claims

Claims 5-6, 15, 30, and 33-34 are currently pending. Claims 1-4, 7-9, 13, 16, 18, 21, 31-32, 35-37, and 39-41 are Canceled. Claims 5-6, 25, 30, and 33-34 are amended. Claim 10-12, 14-15, 17, 19-20, 22, 24-29 and 38 are Withdrawn with the proviso that they been examined once the Independent claims is found allowable.

35 U.S.C. 112, First Paragraph

Claims 5-7, 15, 30, 32-34, 40 and 41

Claims 5-7, 15, 30, 32-34, 40 and 41 have been rejected under 35 U.S.C. 112, first paragraph for failing to comply with the written description requirements. Specifically for the inclusion of the phrase "essentially free of tocotrienols".

The phrase "essentially free of tocotrienols" has been removed from Independent Claim 30. In light of this amendment, the Examiner is requested to remove this rejection and allow the claims.

35 U.S.C. 102(b)

Claims 5-7, 30, 32-34, 40, and 41

Claims 5-7, 30, 32-34, 40, and 41 have been rejected under 35 U.S.C. 102(b) as being anticipated by Alaux et al., Levy et al., Kapadia et al. or JP 2001114628. The Examiner has stated that Alaux, Levy, and Kapadia each teach an annatto extract and JP teaches an oral agent containing an agent from *Bixa orellana*, thus it also teaches an annatto extract.

Independent Claim 30 has been amended to more precisely claim the disclosed composition. The claim has been amended to add two additional limitations. The extract from the annatto seed has been more precisely claimed to be a composition of the 290 - 390 Dalton MW fraction of the byproduct solution of *Bixa orellana* seed components. The phrase "annatto extract" is imprecise and is used by other authors to define a wide array of compositions. The byproduct solution of *Bixa orellana* seed components is obtained after removing the bixins to produce "yellow cake" and has greatly reduced levels of bixins. The byproduct solution is then distilled to obtain a 290 – 390 Dalton MW fraction. The 290 – 390 Dalton MW fraction is the fraction that contains geranyl geraniol.

Although the molecular weights of bixins (390 – 425 Daltons) overlap the molecular weights of tocotrienol and tocopherol (350 – 450 Daltons), their chemical structure [bixins have 4 oxygen groups; tocotrienols and tocopherols have 2 oxygen groups] inhibits their distillation from the byproduct solution of *Bixa orellana* seed components and remain in the residue material (Exhibit 2 – Declaration of Tan).

Support for this limitation can be found in the paragraph inserted after paragraph [0010] by the amendment to the specification in this Response (support for the paragraph is in Exhibit 1) and the Declaration by Barrie Tan (Exhibit 2). The addition of this limitation does not add New Matter. The molecular weights of the various components in *Bixa orellana* seeds are easy to calculate from their structures and are disclosed in several of the references incorporated by reference in the original specification.

Claim 30 has an additional limitation of "a trans-to-cis isomer ratio between 1:100 to 100:1". The ratio of trans- to cis- isomers in the 290 – 390 Dalton MW fraction is effected by the conditions (e.g., temperature) during the distillation process (Exhibit 2 – Declaration of Tan). The Specification discloses several beneficial effects that are obtained by having different ratios of trans- to cis- isomers of geranyl geraniol. This amendment to Claim 30 differentiates the purified claimed geranyl geraniols from the unprocessed *Bixa orellana* seed or the "annatto extracts" disclosed in the references cited by the Examiner.

No New Matter has been added by this amendment. Support can be found in Original Claim 7 which claimed a trans-to-cis isomer ratio of 1:100 to 100:1.

The sections of the cited references have been copied below to enable a discussion of their disclosures.

Alaux et al. (6514531) – Column 8, lines 55 to end. [Emphasis added]

Among suitable colouring excipients the following may be cited: indigotine, cochineal carminic acid, yellow orange S, allura red AC, iron oxides, curcumin, riboflavin, tartrazine, quinoline yellow, azorubine, amaranth, carmines, erythrosine, red 2G, patented blue V, glittering blue FCF, chlorophylls, copper complexes of chlorophylls, green S, caramel, glittering black BN, carbo medicinalis vegetabilis, brown FK and HT, carotenoids, Annatto extracts, paprika extracts, lycopene, lutein, canthaxanthin, beetroot red, anthocyanes, calcium carbonate, titanium dioxide, aluminium, silver, gold or litholrubin BK or any other colouring excipient suitable for an oral administration.

Levy et al. (2003-0104090) – Abstract, paragraph 2 & 7, Ex. 3 [Emphasis added]

Abstract

Methods are provided for eliciting a beneficial health effect in a human or non-human animal which include adding at least one bixin compound or an extract of the annatto (Bixa orellana) seed to an animal feed, food product or nutritional supplement in an amount effective to increase the concentration of bixin in the blood supply of the animal when the food or supplement is consumed at a recommended daily dosage (unit dosage) for a sufficient number of days. A method of eliciting a therapeutic health effect in a human or non-human animal by adding an effective amount of at least one bixin compound to a pharmaceutical compound is also provided. ...

[0002] Annatto extracts are obtained from the seeds of the tropical tree *Bixa orellana*. Annatto seed extracts contain bixin compounds, the isoprenoid geranylgeraniol, the vitamin E tocotrienol, and derivatives and isomers thereof. As used herein, the term "bixin compound" will be understood to refer to bixin per se and/or its derivatives, including salts and isomers thereof, as well as mixtures thereof including those with the other co-extractives from the annatto seed. The bixin compounds include especially compounds having the basic skeletal structure of norbixin, including its monomethyl ester

(bixin), its dimethyl ester (methylbixin), and higher alkyl (e.g., C_{sub.2}-C_{sub.40} alkyl) esters, as well as optical isomers thereof and pharmaceutically and dietary acceptable salts thereof.

[0003] Bixin is found in nature only in the annatto seed in the form of the 9'-cis isomer. It is converted (hydrolyzed) rapidly in the mammalian body to norbixin in the form of the all-trans isomer. Bixin may be purified from the annatto seed by organic solvent extraction and is available commercially as a color additive for foods, usually as a 1.6 wt % solution in soybean oil (known as annatto color E161b). Bixin and methylbixin may also be prepared synthetically, as described in the literature.

EXAMPLE 3

[0050] last sentence - From experience in similar populations as these two patients, the results suggest that the annatto extract treatment decreased lasting and postprandial plasma glucose levels by improving hepatic and peripheral (muscle) tissue sensitivity to insulin.

[0051] It has thus been found, according to the present invention, that bixin compounds and annatto extracts, especially in dosage amounts above the levels normally used for coloring purposes, exert a profound beneficial effect on the health of humans and non-human animals. Bixin compounds may thus be used as nutritional supplements...

[0052] Furthermore, the nutritional supplementation of humans and non-human animals with bixin compounds and other annatto seed extractives has protective and therapeutic health effects. Although a method to separate the components of the annatto seed extract by distillation in order to use these components individually as supplements or as building blocks for chemical synthesis is described in U.S. Pat. No. 6,350,453, according to the present invention the bixin compounds and other annatto seed extractives seem to cause a much more significant synergistic protective and therapeutic health effect when ingested together than when the components are administered individually.

Kapadia et al. (5935581) – Column 7, lines 55-65 [Emphasis added]

Research was also done on natural food colorants extracted from turmeric, annatto seeds, and paprika. These colorants are commercially available in a variety of formulations in aqueous, vegetable oil, or propylene glycol vehicles. These vehicles may also contain emulsifiers and/or dispersants such as polysorbate 80 and lecithin. Recent studies have reported that colorants derived from turmeric, annatto, and paprika inhibit carcinogenesis.....

a) a mixture of natural extractives of annatto seeds and turmeric with polysorbate 80, potassium hydroxide, and propylene glycol; and

b) a natural extractive of paprika in vegetable oil.

JP 2001114628 – abstract [Emphasis added]

An oral agent for changing skin color, contains norbixin (obtained from Bixa orellana) as active component.

All of the cited references disclose use of the colorant - bixins - from annatto seeds. Occasionally the references use the phrase “annatto extract” or variations thereof interchangeably with “Bixins”. A careful reading of the references shows that they are disclosing the use of bixins extracted from annatto seeds, not the geranyl geraniols, tocotrienols and tocopherols which are disclosed and claimed in the application.

Although the phrase of “annatto extract” is used in the present application, its definition and meaning is entirely different from its use in the cited references.

Paragraph [0009] of the application states:

A "byproduct solution of Bixa orellana seed components" is defined herein as a solution derived from Bixa orellana seed components having a concentration of annatto colorant significantly reduced from that of Bixa orellana seeds themselves. Other common terms for byproduct solution used for commercial products include: oil-soluble annatto color or annatto oil. Generally, the concentration of annatto colorant, which is defined as bixins and other carotenoids, chemically modified, altered or esterified, in byproduct

solution of Bixa orellana seed is less than about two percent, by weight, such as between about 0.05 weight percent and about 2.0 weight percent.

Additionally, the “byproduct solution of Bixa orellana seed components” is distilled to obtain a 290 - 390 Dalton MW fraction containing geranyl geraniols. Therefore, the extracts being used in the References and the extracts disclosed and claimed in the application are mutually exclusive compositions, and are not interchangeable.

This point is emphasized in Levy et al. (2003-0104090) paragraph [0052] where they state that it is the bixin compounds that give a protective effect, rather than distilling the annatto seed extract in to its individual components as in U.S. Pat. No. 6,350,453.

In fact, it is the methods disclosed in U.S. Pat. No. 6,350,453 (Barrie Tan -- the same inventor as this application) that serve as the background for this application (Exhibit 2 – Declaration of Tan). Thus, Levy actually teaches against using the “annatto extract” disclosed in this application

In light of the amendments and arguments showing that the cited references do not disclose the claimed composition, the Examiner is requested to remove this rejection and allow the claims.

35 U.S.C. 103(a)

Claims 5-7, 15, 30, 32-34, 40 and 41

Claims 5-7, 15, 30, 32-34, 40 and 41 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Alaux et al., Levy et al., Kapadia et al., or JP 2001114628 taken with JP 62123113, GB 2178662 or WO 89/01740. The Examiner has stated that Alaux et al., Levy et al., Kapadia et al., or JP 2001114628 do not teach CoQ10 added to the composition. However, JP 62123113, GB 2178662 or WO 89/01740 teach the CoQ10 is known to be used in oral compositions.

The discussion above for the 35 U.S.C. 102(b) rejection shows that the references of Alaux et al., Levy et al., Kapadia et al., or JP 2001114628 do not disclose a composition as claimed in the amended claims. The references of JP 62123113, GB 2178662 or WO 89/01740 or their combination with Alaux et al., Levy et al., Kapadia et al., or JP 2001114628 do not cure the deficiencies outlined in the above discussion of the 35 U.S.C. 102(b) rejection.

In light of the amendments and arguments showing that the cited references do not disclose the claimed composition, the Examiner is requested to remove this rejection and allow the claims.

Conclusion

Claims 5-6, 15, 30, and 33-34 are currently pending. Claims 1-4, 7-9, 13, 16, 18, 21, 31-32, 35-37, and 39-41 are Canceled. Claims 5-6, 25, 30, and 33-34 are amended. Claim 10-12, 14-15, 17, 19-20, 22, 24-29 and 38 are Withdrawn with the proviso that they been examined once the Independent claims is found allowable.

The claims have been amended to claim more precisely the disclosed invention. No new matter has been added by the amendments to the claims.

Applicant has endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefore, and arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested and it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Payment is made for an Extension of 1 month for filing this response. No additional fees are believed due; however, please charge any additional fees, including any fees for additional extension of time, or credit overpayment to credit card information.

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